APPENDIX B

STUDY SYNOPSIS

The proposed clinical study is an open label, dose escalating Phase 1 study of G207, a genetically engineered herpes simplex virus type 1, in the treatment of malignant glioblastoma. G207 was derived from the wild-type herpes simplex virus type 1 strain F [HSV-1(F)] by deleting both copies of the γ34.5 neurovirulence gene. The clinical strategy takes advantages of the virus' ability to infect and lyse cells. The TK gene, which confers sensitivity to ganciclovir and acyclovir is intact. The *E. coli lacZ* gene has been inserted into the ICP6 region for use as a readily identifiable marker which differentiates G207 from HSV-1(F).

Preclinical studies in rodents and Aotus monkeys have demonstrated that the approach is both rational and safe.

Approximately twenty-four patients who have failed conventional therapy with radiation and/or chemotherapy will be enrolled in the study. Treatment will consist of a single stereotactic injection of approximately 0.1 mL of G207 into a region of tumor that has been defined by MRI. Higher doses will be achieved by injection of 0.1 mL into multiple loci. The primary purpose of the study is to obtain safety information in small numbers of individuals (three patients per group), with successive groups receiving escalating doses of G207 after appropriate intervals for evaluation of safety. As a secondary objective, patients will be followed serially by MRI for potential clinical response to G207.

Follow-up evaluations will consist of routine laboratory analyses and clinical measurements of neurological function and tumor size. Patients will be followed closely during the planned four day post-treatment hospitalization period. Outpatient follow-up evaluations will be performed at months 1, 3, 6, and 12 subject to disease progression.

Pending demonstration of safety in this Phase 1 study, additional clinical strategies for repeat dosing as well as for combination therapy of G207 with radiation therapy and chemotherapy are contemplated.